taining the vector or vectors or by microprojectile-mediated delivery of the vector into the callus;

(i) culturing said transformed embryogenic callus on selection medium;

(j) culturing said transformed embryogenic callus containing embryos on developmental medium containing an osmotic pressure increasing agent;

(k) culturing said transformed embryos on maturation medium; and

(l) recovering transgenic plants from said transgenic embryos.

REMARKS

Minor amendments have been made to the claims to clarify the wording. No new matter requiring additional search or undue consideration is required.

Errors in specification

The Office Action suggested that the application be reviewed for errors, particularly with regard to claims 101 and 102. The applicants have conflicting copies of the amendment filed 13 April 1999, which introduced claims 101 and 102. Applicants will address these errors when the conflict is resolved. Toward that end, the Applicants request the Patent Office to fax a copy of the 13 April 1999 amendment to the undersigned at the fax number indicated below.

Rejection under 35 U.S.C. § 112, first paragraph

The Office Action asserted that certain of the claims did not recite any particular transformation method. The claims have been amended herein to further clarify the methods of transformation.

With regard to transformation by *Agrobacterium tumefaciens*, the Office Action did not address the applicants' arguments with respect to the art recognized distinctions between *A. rhizogenes* and *A. tumefaciens*; the Office Action merely concluded the arguments were not deemed probative. The applicants do not understand why their arguments are deemed non-probative. Up until this point the only basis for rejecting the claims as non-enabled for the recitation of *A. tumefaciens* has been the alleged failure of Follansbee *et al.* with regard to *A. rhizogenes* (see Paper No. 17, p. 5, first full paragraph and Paper No. 13, p. 3, last paragraph). The applicants' response to each of Papers 13 and 17 directly addresses the issue and demonstrates why Follensbee *et al.*'s teaching regarding

transformation with *A. rhizogenes* is non-predictive with respect to transformation with *A. tumefaciens*. The applicants maintain and reassert these previously proffered arguments.

The Patent Office now asserts a new basis of rejection of the claims as non-enabled for transformation with *A. tumefaciens*, pointing to pages 12-13 of the applicants' 28 November 2000 response and alleging the response asserted inherent unpredictability in applying *Agrobacterium* to poinsettia. This basis of rejection could have been raised previously in the 27 February 2001 Office Action (Paper No. 25). As this is a new ground for rejection that could have been made previously, making the present Office Action final is improper, and, therefore, the Applicants respectfully request that the finality of the present Office Action or, preferably, the rejection be withdrawn.

With regard to the applicants' statement relating to *A. tumefaciens* on pages 12-13 of the applicants' 28 November 2000 response, there is nothing about the statement that suggests that *A. tumefaciens*-mediated transformation is unpredictable. What the applicants said on pages 12-13 that related to *A. tumefaciens* transformation was the following:

> The Office Action relies upon Cheetham as a primary reference to demonstrate an Agrobacterium-mediated transformation method of Euphorbia. Cheetham, however, does not teach or suggest an *A. tumefaciens*-mediated transformation method of Euphorbia that results in a poinsettia plant, as recited by the claims. As the Applicants noted in their December 29, 1998, response, Cheetham teaches at page 513 that "no shooting was ever observed" using the disclosed method.
>
> None of the other references provide any teachings that one skilled in the art would have recognized would overcome the failures of Cheetham to obtain whole transgenic poinsettia plants. Thus, the skilled artisan would not have been motivated to combine the teachings of the other references because there would not have been reasonable expectation of success.
>
> Furthermore, the Applicants' December 1998 Response included an Appendix that contained a statement by one of the authors of Cheetham that despite trying various regimens of hormones to get plant regeneration, it was never achieved. Enclosed herewith is the biography of Pamela J. Weathers, the author of the statement and co-author of Cheetham *et al.*, which identifies Dr. Weathers as being of at least ordinary skill in the art. Thus, this statement, demonstrating failure of others to obtain whole transgenic poinsettia plants, is strong evidence of the non-obviousness of the claims.

This is not an argument that *A. tumefaciens*-mediated transformation is unpredictable. Rather, it is an argument that Cheetham *et al.*, both alone and in combination with other art, fails to teach *A. tu-*

mefaciens-mediated transformation of poinsettia. The prior art failure is not due to any unpredictability of *A. tumefaciens* but to the failure to employ the applicants' invention.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 39 and 103 (and those depending from them) were rejected for the recitation "culturing callus produced on medium X on medium Y" in parts (g) of each. The claims have been amended to further clarify the meaning. The applicants thank the Examiner for his suggestions.

Rejections under 35 U.S.C. § 103

The Patent Office maintained the rejection of the claims as obvious.

The prior art fails to teach or suggest the particular multi-step processes for regeneration and for combined transfection and regeneration. For example, claim 1 recites a method comprising:

(a) incubating poinsettia plant tissue explants that produce reddish epidermal callus on auxin- and cytokinin-containing callus induction medium;

(b) subculturing reddish epidermal callus to embryo induction medium comprising casein hydrolysate and NH_4^+ and/or NO_3^- to form embryogenic callus;

(c) culturing said embryogenic callus on developmental medium containing an osmotic pressure increasing agent and cytokinin;

(d) culturing said embryogenic callus on maturation medium comprising abscisic acid; and

(e) recovering poinsettia plants from said embryos.

Each of the claimed methods of producing transgenic poinsettia's also recite these actions.

By contrast Priel *et al.* (p. 50, 1st column) teaches placing stem segments on "callus induction medium" followed by transfer to "somatic embryogenesis induction medium" where, after transfer to fresh medium, the first embryogenic structures become visible. The embryogenic structures are then placed on "somatic embryo maturation medium, where they reach the cotyledonary stage. Neither Priel nor the other cited art teach or suggest placing the embryogenic callus on <u>both</u> a developmental medium <u>and</u> a maturation medium; Priel teaches only placing the embryogenic structures on a maturation medium. Thus, even were one to combine the teachings of the prior art, one would not arrive at the instantly claimed methods.

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Furthermore, the present specification notes at page 16, lines 7-9, that "[t]his additional treatment improves embryo germination uniformity and confers a high degree of desiccation tolerance." This inherent advantage in the presently claimed methods is neither taught or suggested by the cited art.

There is also nothing in the prior art that suggests to the ordinary artisan the other inherent advantages of the presently claimed methods. For example, page 15 of the present specification states that the presently claimed methods are genotype-independent of producing large quantities of somatic embryos of improved quality and yield. Such inherent properties of the present methods were not recognized in the art.

The Patent Office dismissed the applicants' argument that the present methods were genotype-independent, arguing that such methods rely upon high levels of a particular osmoticum and high levels of particular nitrogen source. There is no basis for such an assertion, however.

The Patent Office maintains that the use of casein hydrolysate as a tissue culture medium addition is well known, yet no teaching or suggesting has been provided for its use in poinsettia somatic embryogenesis.

The Patent Office has relied on Nataraja *et al.* for the use of casein hydrolysate in embryo culture medium for poinsettia. The Patent Office correctly notes Nataraja *et al.*'s use was for zygotic rather than somatic embryos, but concludes that one skilled in the art would have recognized that it could be used equally well with each type of embryo. No evidence in support for this assertion has been provided.

As to the other media components, the Patent Office alleges they are well known, yet no evidence in support of this assertion has been provided.

There is simply no teaching or suggestion to make the various *combination* of modifications to prior art methods of *in vitro* regeneration of poinsettia as presently claimed. One cannot establish a *prima facie* case of obviousness without identifying in the art suggestion or motivation to make the *particular* invention being claimed. *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995) ("A general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out."); and *Ex parte Obukowicz*, 27 U.S.P.Q.2d, 1063, 1065 (Bd. Pat. App. Int.

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1992) (Prior art "that gives only general guidance and is not at all specific as to the particular form of the claimed invention and how to achieve it . . . does not make the invention obvious.").

In summary, the applicants respectfully submit that the present obviousness rejections are based on a combination of references that cannot render the presently claimed methods obvious because even when combined, they fail to teach or suggest the use of both a developmental medium and a maturation medium; nor does the prior art teach or suggest the inherent advantages in using both media as recognized by the applications.

Furthermore, the applicants respectfully submit that the Patent Office has relied on particular teachings that were selectively chosen without any suggestion in the references themselves to make such selections. Other differences of the presently claimed method from the prior art have been written off as well known, yet no documentary evidence has been supplied. Furthermore, even were each individual modification suggested, the art as a whole fails to suggest the *combination* of modifications presently recited in the claims. That is, the art fails to suggest the invention as a whole. Lastly, the art fails to provide teachings rendering obvious to one of ordinary skill in the art the inherent advantageous properties of the presently claimed methods.

For all of the foregoing reasons, the applicants respectfully request reconsideration and withdrawal of the § 103 rejections.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

Date: October 9, 2001

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CLAIMS FOR APPLICATION SERIAL NO. 08/903,944

Redlined Version of Amended Claims

6. (Four Times Amended) A method for producing transgenic poinsettia plants, comprising:

(a) incubating poinsettia plant tissue explants that produce reddish epidermal callus on auxin- and cytokinin-containing callus induction medium;

(b) culturing reddish epidermal callus on embryo induction medium comprising casein hydrolysate and NH_4^+ and/or NO_3^- to form embryogenic callus;

(c)

(i) introducing an expression vector into said incubating embryogenic callus to produce transformed embryogenic callus, wherein said expression vector comprises a selectable marker gene and a second foreign gene, or

(ii) introducing two expression vectors into said incubating embryogenic callus to produce transformed embryogenic callus, wherein one of said expression vectors comprises a selectable marker gene, and wherein the second of said expression vectors comprises a second foreign gene;

-wherein the vector or vectors of (c)(i) and (c)(ii) are introduced into the incubating embryogenic callus by co-incubating the callus with *Agrobacterium tumefaciens* containing the vector or vectors or by microprojectile-mediated delivery of the vector into the callus;

(d) culturing said transformed embryogenic callus on selection medium;

(e) culturing said transformed embryogenic callus containing embryos on developmental medium containing an osmotic pressure increasing agent;

(f) culturing said transgenic embryos on maturation medium; and

(g) recovering transgenic plants from said transgenic embryos.

39. (Five Times Amended) A method for producing transgenic poinsettia plants, comprising:

(a) incubating poinsettia plant tissue explants that produce reddish epidermal callus in auxin- and cytokinin-containing callus induction medium;

(b) subculturing embryogenic callus produced on said callus induction medium to liquid NH_4^+ and/or NO_3^- containing embryo induction medium;

(c) filtering the culture and culturing the filtrate in fresh liquid embryo induction medium;

(d) filtering the culture and culturing the filtrate on solid embryo induction medium;

(e) subculturing embryos produced on said embryo induction medium to maturation medium;

(f) culturing said embryos on callus induction medium;

(g) subculturing epidermal callus produced on said callus induction medium ~~on~~ to embryo induction medium to form embryogenic callus;

(h)

(i) introducing an expression vector into said embryogenic callus to produce transformed embryogenic callus, wherein said expression vector comprises a selectable marker gene and a second foreign gene, or

(ii) introducing two expression vectors into said embryogenic callus to produce transformed embryogenic callus, wherein one of said expression vectors comprises a selectable marker gene, and wherein the second of said expression vectors comprises a second foreign gene;

wherein the vector or vectors of (c)(i) and (c)(ii) are introduced into the incubating embryogenic callus by co-incubating the callus with *Agrobacterium tumefaciens* containing the vector or vectors or by microprojectile-mediated delivery of the vector into the callus;

(i) culturing said transformed embryogenic callus on selection medium;

(j) culturing said transformed embryogenic callus containing embryos on developmental medium containing an osmotic pressure increasing agent;

(k) culturing said transformed embryos on maturation medium; and

(l) recovering transgenic plants from said transgenic embryos.

102. (Three Times Amended) A method for producing transgenic poinsettia plants comprising the steps of:

(a) incubating poinsettia plant tissue explants that produce epidermal callus on auxin- and cytokinin-containing callus induction medium;

(b) subculturing embryogenic callus to embryo induction medium comprising casein hydrolysate and NH_4^+ and/or NO_3^- to form embryogenic callus containing embryos;

(c)

(i) introducing an expression vector into said incubating embryogenic callus to produce transformed embryogenic callus, wherein said expression vector comprises a selectable marker gene and a second foreign gene, or

(ii) introducing two expression vectors into said incubating embryogenic callus to produce transformed embryogenic callus, wherein one of said expression vectors comprises a selectable marker gene, and wherein the second of said expression vectors comprises a second foreign gene;

wherein the vector or vectors of (c)(i) and (c)(ii) are introduced into the incubating embryogenic callus by co-incubating the callus with *Agrobacterium tumefaciens* containing the vector or vectors or by microprojectile-mediated delivery of the vector into the callus;

(d) culturing said transformed embryogenic callus on selection medium;

(e) culturing said embryogenic callus containing embryos on developmental medium containing an osmotic pressure increasing agent;

(f) culturing said transgenic embryos on maturation medium; and

(g) recovering transgenic plants from said transgenic embryos.

103. (Twice Amended) A method for producing transgenic poinsettia plants comprising the steps of:

(a) incubating poinsettia plant tissue explants that produce epidermal callus on auxin- and cytokinin-containing callus induction medium;

(b) subculturing embryogenic callus produced on said callus induction medium to liquid embryo induction medium comprising casein hydrolysate and NH_4^+ and/or NO_3^-;

(c) filtering the culture and culturing the filtrate in fresh liquid embryo induction medium;

(d) filtering the culture and culturing the filtrate on solid embryo induction medium;

(e) subculturing embryos produced on said embryo induction medium to maturation medium;

(f) culturing said embryos on callus induction medium;

(g) subculturing embryogenic callus produced on said callus induction medium ~~on~~ to embryo induction medium to form embryogenic callus containing embryos;

(h)

(i) introducing an expression vector into said incubating embryogenic callus to produce transformed embryogenic callus, wherein said expression vector comprises a selectable marker gene and a second foreign gene, or

(ii) introducing two expression vectors into said incubating embryogenic callus to produce transformed embryogenic callus, wherein one of said expression vectors comprises a selectable marker gene, and wherein the second of said expression vectors comprises a second foreign gene;

wherein the vector or vectors of (h)(i) and (h)(ii) are introduced into the incubating embryogenic callus by co-incubating the callus with *Agrobacterium tumefaciens* containing the vector or vectors or by microprojectile-mediated delivery of the vector into the callus;

(i) culturing said transformed embryogenic callus on selection medium;

(j) culturing said transformed embryogenic callus containing embryos on developmental medium containing an osmotic pressure increasing agent;

(k) culturing said transformed embryos on maturation medium; and

(l) recovering transgenic plants from said transgenic embryos.